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Best evidence topic

Laparoscopic common bile duct exploration versus pre or post-operative ERCP for common bile duct stones in patients undergoing cholecystectomy: Is there any difference?

R. Kenny [a], J. Richardson [b], E.R. McGlone [a], M. Reddy [a], O.A. Khan [a, *]

[a] Department of Upper GI Surgery, St George's Hospital, London, UK
[b] Department of Surgery, Southampton General Hospital, Southampton, UK

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ABSTRACT

A best evidence topic in surgery was written according to a structured protocol. The question addressed was: in patients with symptomatic gallstones and concomitant common bile duct (CBD) stones, is a single-stage surgical strategy (laparoscopic cholecystectomy (LC) with common bile duct exploration) preferable, or a two-stage procedure involving LC with pre or post-operative endoscopic retrograde cholangiography (ERCP)? Two hundred and six papers were found using the reported search, of which four presented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group, study type, relevant outcomes and results of these papers are tabulated. A recent large meta-analysis concluded no significant difference in the clinical effectiveness or complication rate of either strategy. Three recent smaller studies concurred with this conclusion; however each noted improved cost-effectiveness of the single-stage approach advocating its use as the superior strategy when local resources and expertise are available.

We conclude that for patients with symptomatic gallstones and concomitant choledocholithiasis, a single-stage surgical procedure is equivalent to two-stage LC and ERCP in terms of clinical outcomes, is associated with a shorter overall hospital stay and may be more cost-effective. On this basis a single-stage procedure is recommended for management of symptomatic gallstones and choledocholithiasis where local resources and expertise permit.

1. Introduction

In most UK hospitals there are two broad options for management of patients found to have choledocholithiasis during investigations for symptomatic gallstones: a solely surgical strategy which comprises laparoscopic cholecystectomy (LC) and clearance of CBD stones in one sitting, or a two-stage approach consisting of LC and pre- or post-operative ERCP. In order to investigate which is preferable, a Best Evidence Topic was constructed according to a structured protocol as described in a previous publication by the IJS [1]. This is a validated method of appraising current evidence to answer relevant clinical questions.

2. Clinical scenario

You are at a management meeting discussing ways to save money within the department. It is noted that patients requiring cholecystectomy as well as clearance of CBD stones usually undergo two procedures (LC followed or preceded by ERCP), and it is proposed that suitable patients could instead be treated at a single sitting. You are competent to perform laparoscopic exploration of common bile duct (LCBDE), but are uncertain if this leads to improved outcomes or cost-effectiveness. You resolve to check the literature to determine the relative efficacy and cost-effectiveness of the single-stage surgical and two-stage strategies.

3. Three-part question

In patients found to have CBD stones in addition to gallstones, is a single-stage superior to two-stage strategy for stone clearance?

* Corresponding author. Department of Surgery, St George's Healthcare NHS Trust, Blackshaw Road, London, SW17 0QT, UK.
E-mail addresses: rosskenny@doctors.org.uk (R. Kenny), okhan342@gmail.com (O.A. Khan).

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Table 1
Best evidence papers.

Author, date and country, study type and level of evidence	Subject group	Outcomes	Key results	Comments
Lu et al. (2012) *World Journal Gastroenterology* (China) Meta-analysis Level Ia	Seven eligible RCT's comprising of 787 patients. 5 trials ($n = 621$) compared preoperative ERCP + LC with LC + LCBDE. 2 trials ($n = 166$) compared LC + LCBDE with LC + post-operative ERCP. Group 1: Two stage pre/post-operative ERCP + LC Group 2: Single stage LC + LCBDE	Successful duct clearance Post-operative morbidity Conversion to other procedures Total operative time Length of hospital stay	Group 1: 78.8% Group 2:87.2% $p = 0.17$ Group 1: 15.2% Group 2: 19.0% $p = 0.16$ Group 1:13.9% Group 2: 12.0% $p = 0.39$ No statistically significant difference between the two groups (MD = 12.14, 95% CI: −1.83 to 26.10, $p = 0.09$) No statistically significant difference between the two groups (MD = 0.99, 95% CI: −1.59 to 3.57, $p = 0.45$)	This was a well conducted large study looking at short term outcomes between the two groups. Authors concluded that single stage management is equivalent to two stage management, with the decision for either dependent on local resources and expertise. This study is limited in the heterogeneity that exists between trials and likely publication bias
Bansal et al. (2014) *Surgical Endoscopy*, (USA) [5] Prospective randomized control trial Level 1b	From February 2009 to October 2012, 168 patients were randomized: 84 to the single stage procedure (group 1) and 84 to the two stage procedure (group 2). Both groups were matched with regard to demographic and clinical parameters.	Successful CBD exploration Successful CBD clearance Mean operative time (min) Overall hospital stay (days) Average cost of procedure per patient (US $) Incremental cost-effectiveness ratio (US $)	Group 1: 91.7% Group 2: 88.1% $p = 0.22$ Group 1: 88.1% Group 2: 79.8% $p = 0.069$ Group 1: 135.7 ± 36.6 Group 2: 72.4 ± 27.6 $p < 0.001$ Group 2 significantly shorter operative time Group 1: 4.6 ± 2.4 Group 2: 5.3 ± 6.2 $p = 0.03$ Group 1 significantly shorter hospital stay Group 1: $394.1± $133.1 Group 2: $506.5± $235.3 $p < 0.001$ Group 1 significantly lower cost of procedure $-1182.7 − This indicates the single stage laparoscopic CBD exploration more effective and less costly than the two stage procedure.	This was a well conducted large study looking at short term outcomes between the two groups. The two stage procedure was significantly more expensive ($p < 0.001$) but there was no significant difference between the two groups in terms of wound infection rate or major complications. Limitations exist in that LCBDE was performed almost entirely via choledochotomy and not transcystically leading to increased operative time and bile leak. The cost-effectiveness ratio used does not take into account quality of life and the results of such a composite variable may not be generalisable, as they depend on relative costs of resources and complication rates which vary between centres.
Lu et al. (2013) *American Surgeon* (USA) Retrospective case control study Level IIb	One-stage versus two stage management for concomitant gallbladder stones and common bile duct stones in patients with obstructive jaundice. One-stage management ($n = 88$) or two stage management ($n = 122$) was used for 210 eligible patients between January 2009 and March 2011.	Stone clearance from the common bile duct (CBD) Post-operative morbidity Mortality Conversion to open Operative time (min) Length of stay (days) Cost-effectiveness 1 Surgical charges 2 Total charges	One-stage: 93.2% Two stage: 95.1% $p = 0.28$ One stage: 10.2% Two stage: 15.6% $p = 0.12$ One stage: 0.0% Two stage: 0.8% $p = 0.16$ One stage: 6.8% Two stage: 9.8% $p = 0.21$ One stage: 98.7 ± 9.7 Two stage: 126.9 ± 19.5 $p < 0.001$ One stage significantly shorter One stage: 5.1 ± 2.5 Two stage: 7.9 ± 3.9 $p < 0.001$ One stage significant shorter One stage: 1 $921 ± $127.1 2 $1310.5 ± $199.4 Two stage: 1 $3473.1 ± $1116.3 2 $4157.8 ± $1106.0	This was a well conducted large study looking at short term outcomes between the two groups. One-stage management was more cost-effective and decreased the number of procedures. In addition, post-operative hospital stay and operative time were shorter for patients who received one-stage management. This paper is limited by surgeon bias within the same centre as to choice of management.

Table 1 (*continued*)

Author, date and country, study type and level of evidence	Subject group	Outcomes	Key results	Comments
			$p < 0.001$ (for both 1 & 2) One stage significantly more cost-effective	
Topal et al. (2010) *Surgical endoscopy* (Netherlands) Retrospective case control study Level IIb	Between October 2005 and September 2006 53 patients presenting with symptoms of gallstone disease were managed for CBD stones with either a one or two stage procedure 38 patients were identified as eligible for cost analysis Group 1 (19 patients): One stage procedure Group 2 (19 patients): Two stage procedure	Hospitalisation cost (€) Operation costs (€) Medical staff costs (€) Paramedical staff costs (€) Pharmacy/ consumables cost (€)	Group 1: 701 (0–2599) Group 2: 2190 (723–4471) $p < 0.0001$ Group 1: 1278 (616–1884) Group 2: 1232 (720–2356) $p = 0.280$ Group 1: 638 (313–994) Group 2: 720 (443–1133) $p = 0.062$ Group 1: 1035 (299–1875) Group 2: 1860 (923–2973) $p = 0.0002$ Group 1: 645 (185–1013) Group 2: 1476 (298–2193) $p < 0.0001$	This was a well conducted small study looking at hospitalization costs categories between the two groups. This paper concludes that the management of concomitant CBD and gallstone disease should be single stage providing local expertise is available, based on significantly reduced costs compared to the two stage procedure. This paper is limited by its small sample size (19 patients in each) and by the fact that cost data determined is difficult to compare internationally with respect to large diversities within healthcare systems, socio-economic aspects and insurance policies.

4. Search strategy

Medline 1990 to March 2014 using the PUBMED interface for the term: ('Common bile duct' [MeSH] OR CBD) AND (stone OR 'calculi' [MeSH]) AND (laparoscopic cholecystectomy OR 'laparoscopy' [MeSH]) AND ('cholangiopancreatography' [MeSH] OR 'endoscopic retrograde' [MeSH] OR ERCP). The search was filtered for English articles to include meta-analyses, randomised and non-randomised control trials, systematic reviews and comparative studies. The reference lists for articles identified as relevant were also reviewed. The search was valid as of 8th of April 2014.

5. Search outcome

Two hundred and six papers were found using the reported search. One hundred and twenty-five papers were irrelevant; 26 papers were excluded because they were not in English, 28 papers were technical reports describing surgical techniques, nine papers were case reports and six papers investigated the diagnosis of CBD stones. Of the remaining 12 papers, seven relevant randomised control trials were covered by a single meta-analysis, and one was a systematic review superseded by the meta-analysis previously identified. Three further papers, one randomised control trial and two case control studies were identified as representing the best evidence to answer this clinical question (Table 1) [2–5].

6. Results

Please refer to Table 1: Best evidence topics.

7. Discussion

The prevalence of patients awaiting laparoscopic cholecystectomy for symptomatic gallstone disease who also have concomitant CBD stones is 3–10% [2]. There are three options for the management of such CBD stones; (i) conservative management (ii) surgical exploration of the CBD with stone retrieval or (iii) ERCP. Conservative management is reserved for non-obstructing CBD stones, with one third estimated to pass spontaneously within six weeks of cholecystectomy [6]. For obstructing CBD stones, intervention is required. A single-stage surgical strategy with LCBDE and stone retrieval at the time of LC has the advantage of significantly shorter overall hospital stay [4]. An alternative option is two-stage surgical and endoscopic management, with LC and ERCP on separate dates for CBD stone clearance. An advantage of this approach is significantly shorter surgical time [3], but patients are exposed to the risks associated with ERCP such as pancreatitis in up to 5% [7], and delays between the two-stages of treatment may result in prolonged hospital admission [3].

Lu et al. [2] in 2012 performed a meta-analysis to compare clinical outcomes of one-stage LCBDE at the time of LC versus two-stage LC preceded or followed by ERCP and clearance of common bile duct stones. Seven trials with 787 patients were included, with a total of 387 patients undergoing a single-stage surgical procedure for stone clearance and 400 patients a two-stage LC with pre- or post-operative ERCP. Inclusion criteria for all randomised controlled trials required patients to have symptomatic gallstones and to be suspicious for, or proven to have, CBD stones based on clinical presentation (jaundice, cholangitis, pancreatitis), deranged liver function tests or imaging (ultrasound, MRCP or intraoperative cholangiography). Outcomes measured were successful duct clearance, mortality, post-operative patient morbidity, conversion to other procedure, total operative time and length of hospital stay. For none of these variables was there a statistically significant difference when comparing a single versus two-stage management strategy (Table 1).

Lu's meta-analysis is a comprehensive review of the evidence available at the time of publication; however, as with any meta-analysis, it is limited by the quality of the seven papers on which it is based. The majority of these studies are underpowered, with all but two studies having 50 patients or less in each arm. They are also likely to be subject to publication bias, with asymmetry shown in the funnel plot analysis, and there is statistical heterogeneity between their measurements. The systematic review also only included trials published in English.

Since Lu's meta-analysis two large studies have taken place adding 378 patients to the evidence base. In 2014, Bansal et al. [3] performed a randomised controlled trial to investigate the effect of single versus two-stage strategies for the treatment of symptomatic gallstones and concomitant CBD stones. One hundred and sixty eight patients confirmed on imaging to have concomitant CBD and gallstones were randomised to either single-stage LCBDE and LC (group 1) or ERCP for endoscopic extraction of the CBD stones followed by LC (group 2). Success was defined as LC and complete clearance of CBD by intended method. In addition a number of secondary outcomes were measured, including cost effectiveness

which was measured using the incremental cost-effectiveness ratio, calculated as the (average cost of single-stage − average cost of two-stage) divided by (average effect of single-stage − average effect of two-stage). The average effect of each group was calculated by dividing the total number of patients with an uneventful post-operative course by the total number of patients in each group [3].

This study concluded that LCBDE trended to having a higher overall success rate as compared to the two-stage procedure, although this was not statistically significant ($p = 0.069$). LCBDE as a single-stage strategy was shown to result in significantly shorter overall hospital stay ($p = 0.03$), and was associated with significantly reduced cost total cost ($p < 0.001$) despite significantly increased operating time ($p < 0.001$). Within the discussion, the authors explain that the major contributory factors to influence cost are operative time, length of hospital stay, number of procedures and rate of complications. This paper is the first to include a cost-effectiveness analysis as of the single surgical compared to two-stage strategies for patients' requiring both LC and CBD stone clearance. The results of such a composite variable may not be generalisable, as they depend on relative costs of resources and complication rates which vary between centres. An additional limitation of this study is that although LCBDE may be performed via choledochotomy or via a trans-cystic approach, with each technique carrying separate risk profiles, almost all LCBDE in this study were performed via choledochotomy. The authors suggest that a higher rate of bile-leak in the single-stage cohort as compared to the two-stage group may be due to this choledochotomy technique of LCBDE however this cannot be demonstrated by their data. Tokumura et al. [8] in 2002 found trans-cystic approach to be associated with reduced morbidity (notable less frequent bile leakage) and shorter hospital stay compared to choledochotomy.

Lu et al. [4] in 2013 followed on from their previous meta-analysis [2] by performing a retrospective study evaluating the effectiveness and safety of a one-stage (LC plus LCBDE) versus two-stage (ERCP and LC) strategy for patients with symptomatic gallstones and concomitant choledocholithiasis. Two hundred and ten eligible patients underwent one-stage ($n = 88$) or two-stage ($n = 122$) management strategies. No significant difference was observed for the outcomes of CBD stone clearance, post-operative morbidity, mortality and conversion to open surgery. A one-stage strategy was shown to have significantly lower surgical ($921 vs $3473.1) and total cost ($1310.5 vs $4157.8) in comparison to a two-stage strategy ($p < 0.001$).

This study was non-randomised and despite being from a single institution, both cohorts were well matched in terms of pre-clinical characteristics. Its limitations are inherent to its design; decisions for treatment strategy were made by five surgeons operating within a single centre, according to individual preference and thus susceptible to bias. Cost-effectiveness was approximated by the cost of surgical charges and total charges in US dollars, however no description of how these costs were calculated, or how they correlate to cost effectiveness is mentioned.

Topal et al., in 2010 [5] looked specifically at the issue of cost variance between one and two-stage management of common bile duct stones. In 335 consecutive patients between October 2005 and September 2006 presenting with symptoms of gallstone disease, 53 were managed for CBD stones with either a one or two-stage procedure. Decision for therapeutic intervention was based on logistic reasons at the time of presentation, with expertise available in both ERCP and LCBDE throughout. Exclusion criteria consisted patients transferred from another unit (three), ERCP post laparoscopic cholecystectomy (one) and post-operative complications after either ERCP or LCBDE (three and four respectively). 38 patients were identified as eligible for cost analysis: 19 one-stage management and 19 two-stage management patients. Cost analysis started at the time of admission and ended at the time of discharge. A cost accounting model was developed based on the concept of activity-based costing; hospital activities were allocated into 'cost centres' with different cost categories within each activity linked to the individual patient via the 'bill of activities'. Cost drivers were identified at each cost centre assumed to be most responsible for costs, with all costs (direct and indirect) linked to the individual patient according to these drivers. Costs were calculated in euros.

Costs per patient were significantly less after a one-stage versus two-stage procedure ($p < 0.0001$). Operation costs were found to be not statistically different ($p = 0.28$) however hospitalization costs ($p < 0.0001$), pharmacy costs ($p < 0.0001$) and para-medical personnel costs ($p = 0.0002$) were all significantly reduced for the one-stage procedure.

This paper concludes that the management of concomitant CBD and gallstone disease should be single-stage providing local expertise is available, based on significantly reduced costs compared to the two-stage procedure. This paper is limited by its small sample size (19 patients in each) and by the fact that cost data determined is difficult to compare internationally with respect to large diversities within healthcare systems, socio-economic aspects and insurance policies.

A meta-analysis performed by Alexakis et al., in 2012 [9] examining single versus two-stage approaches for the treatment of choledocholithiasis included trials in which the single-stage strategy consisted of LC plus intraoperative ERCP. It concluded that single-stage and two-stage strategies are equivocal in terms of clinical outcomes but more research is needed into long term outcomes such as quality of life, and cost effectiveness. Intra-operative ERCP is a procedure performed very rarely in the UK largely due to the need for the equipment and expertise of both a surgeon and gastroenterologist in the same sitting, and for this reason has not been included in the present analysis.

In conclusion the Lu meta-analysis performed in 2012 [2] indicates that there is no significant difference in the clinical outcomes of a single-stage surgical strategy for the removal of CBD stones versus a two-stage strategy. This is a conclusion that has been reinforced by subsequent studies. However, more recent evidence cites additional benefits of a single-stage strategy in terms of both cost and length of hospital stay [3–5]. There is a need for further research into the health economics and quality of life variables within this field.

8. Clinical bottom line

A single-stage surgical versus two-stage strategy in the treatment of concomitant CBD and gallstone disease has been shown to be equivalent in terms of clinical complications. The single-stage approach has been shown to carry greater cost-effectiveness with reduced length of hospital stay and on this basis should be the preferred procedure where resources and local expertise are available.

Ethical approval

None required.

Author contribution

Kenny R – Study design, data collection, data analysis, writing.
Richardson J – Study design, data collection.
McGlone ER – Critical revision for intellectual content.
Reddy M – Critical revision for intellectual content.
Khan OA – Critical revision for intellectual content.

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